

Objective:

Waning immunity and emergence of SARS-CoV-2 variants impact COVID-19 vaccine efficacy. Here, we studied longitudinally the humoral response induced by Pfizer, AstraZeneca, Janssen, Coronavac and Sputnik Vaccines, with or without booster doses. We also asked how breakthrough Omicron infection in Pfizer-vaccinated individuals enhances antibody levels and cross-reactivity.

Methods:

We analyzed 349 sera from individuals immunized with five vaccines, Pfizer/BioNTech (BNT162b2), AstraZeneca (ChAdOx1 nCoV-19), Janssen (Ad26COV2.S), Sinovac biotech (Coronavac) or Sputnik (Gam-COVID-Vac). We also examined in 92 sera the impact of a Pfizer booster dose in individuals immunized with Pfizer, Janssen or Sinovac regimens. Samples were collected up to 15 months after the first injection, and 5 months after the boost. We measured anti-S antibodies by flow cytometry with the S-Flow assay, and neutralization titers against infectious D614G, Alpha, Beta, Delta and Omicron isolates.

Results:

Administration of two doses of Pfizer, AstraZeneca, Sputnik vaccines, or an heterologous AstraZeneca/Pfizer regimen, induced seroconversion of 100% of individuals and neutralization activity against D614G, Alpha, Beta and Delta, but not Omicron. Janssen and Sinovac vaccines elicited lower levels of anti-S antibodies, and no detectable neutralization of Delta and Omicron. During the first 8 months, the antibody levels and neutralization activity progressively declined with all vaccines. A booster dose of Pfizer strongly increased antibody response and elicited neutralizing antibodies against Omicron. However, titers were 8- to 36- fold lower against Omicron relative to Delta. We observed a waning of the humoral response after the boost and estimated that neutralizing antibodies against Omicron will no longer be detectable in the sera after 7 months. Breakthrough Omicron infections strongly increased the levels of cross-reactive antibodies with titers only 2.5-fold lower against Omicron compared to Delta.

Table 1: Study participants

	Pfizer	AstraZeneca Pfizer	AstraZeneca (2 doses)	Janssen	Sputnik	Sinovac
	n=44	n=11	n=23	n=18	n= 62	n=26
Sex						
Female	23	6	14	12	7	12
Male	21	5	7	9	7	9
Age (Median; range)	59 (29;81)	38 (29 ;50)	59 (55;73)	57 (55 ;79)	48 (31 ;61)	32 (24 ;64)
Immune deficiency	0	0	0	0	0	0
Previous COVID-19	0	0	0	0	0	0
Anti-N	0	0	0	0	0	Not done
1st dose	Jan 4 - 8, 2021	Feb 9 - Mar 4, 2021	Feb 5 - Apr 7, 2021	June 16 - 25, 2021	Feb 2 - July 20, 2021	Feb 9 - 18, 2021
2nd dose	Jan 20 - Feb 5, 2021	Apr 16 - 26, 2021	May 3 - 19, 2021		Feb 23 - Aug 10, 2021	Mar 3 - 10, 2021
Booster dose	Aug 31 -Sept 6, 2021			Sep 17 - Dec 4, 2021		Oct 4 -20, 2021

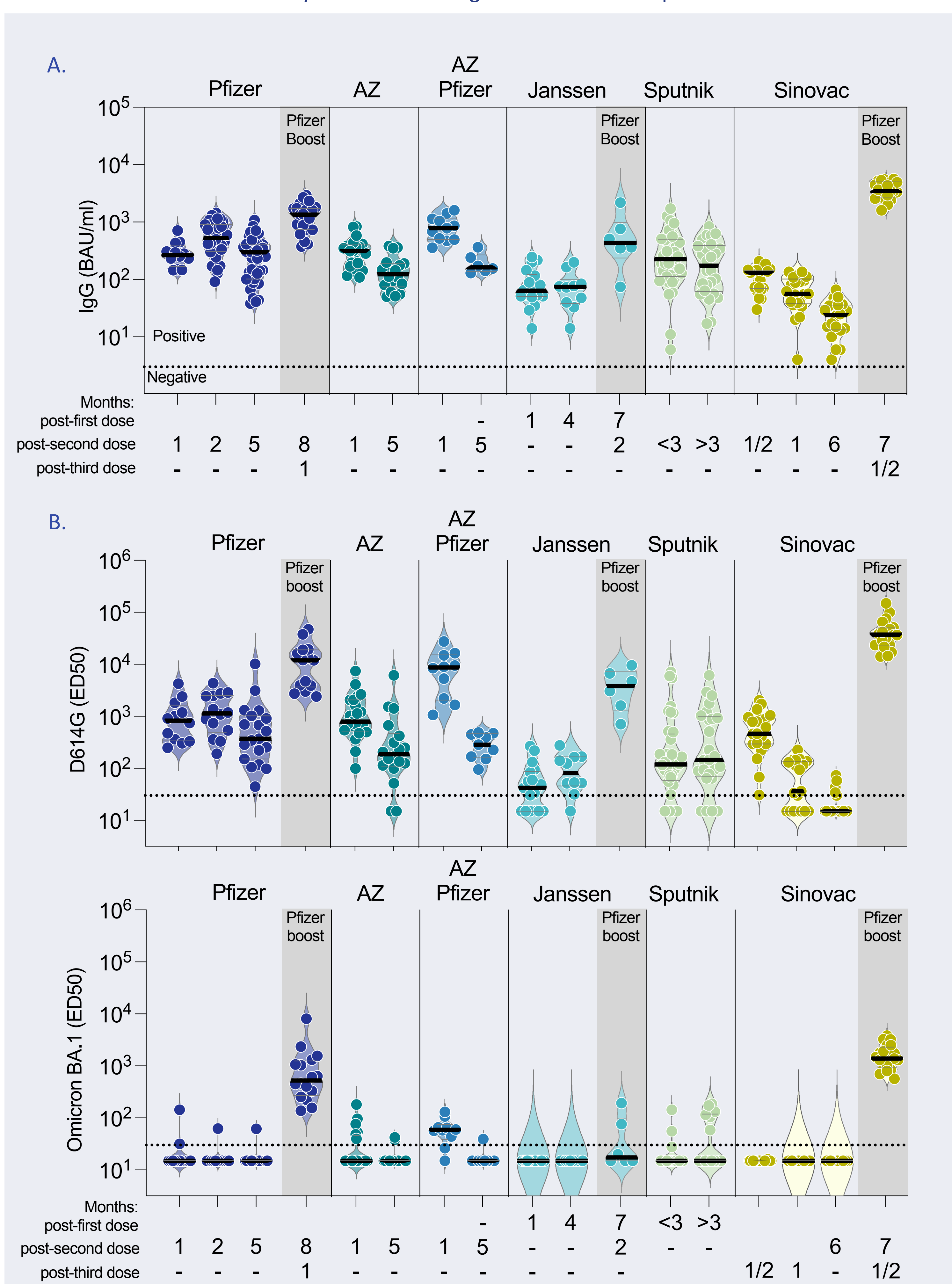


Figure 1: Comparison of anti-S antibody levels and neutralizing antibody titers induced by different vaccines.

Sera from vaccinated individuals from different cohorts were collected. Months post first and second doses are indicated in the x-axis.

(A) Shown are the levels of anti-S immunoglobulin G (IgG) antibodies in BAU/ml.

(B) Shown are live SARS-CoV-2 neutralization titers (ED50) against D614G and Omicron BA.1. The black dotted line indicates the limit of detection (BAU/ml=3; ED50=30).

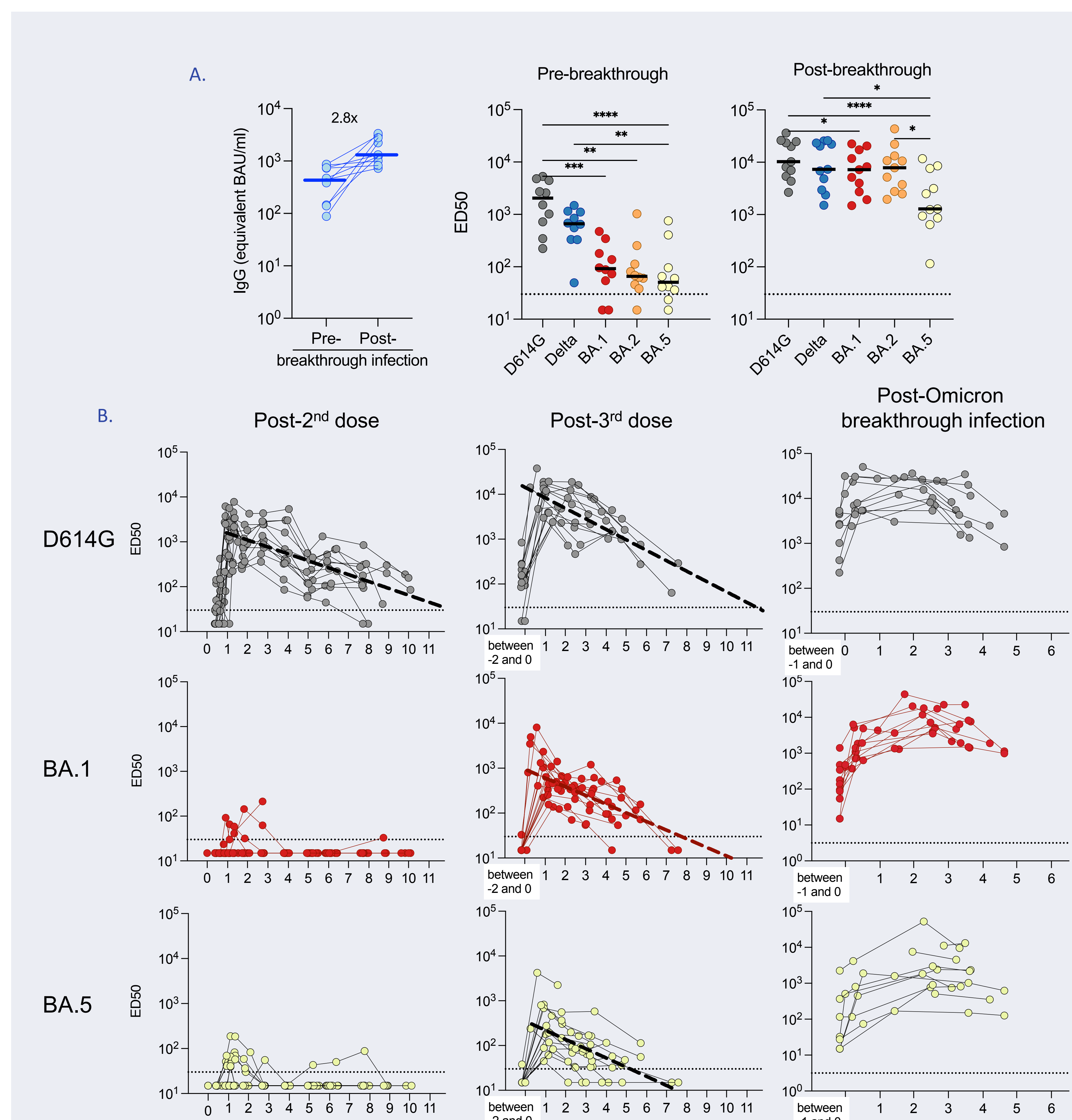


Figure 2: Temporal evolution of the neutralization profile.

(A) Level of anti-Spike IgG and cross-neutralization profile in vaccine recipients, with or without breakthrough Omicron BA.1/BA.2 infection.

(B) Longitudinal analysis of the evolution of serum cross neutralization, up to 16 months after initiation of the vaccination.

The black dotted line indicates the limit of detection (BAU/ml=3; ED50=30).

Conclusion:

Our results highlight differences between vaccines and support the use of an mRNA-based vaccine as a booster regardless of prior regimens.

The duration of the neutralizing humoral response after the boost is estimated to be about 7 months. A high level of cross-reactivity is observed in Omicron breakthrough cases.

Our data suggest that an Omicron-specific booster may improve cross-immunity.

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